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An observational cohort study to determine efficacy, adherence and outcome of the early initiation of pressure support ventilation during mechanical ventilation

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ABSTRACT

Background: Timely initiation of weaning from mechanical ventilation (MV) is important. Non-validated screening criteria may delay weaning if too prescriptive. This study observed physician-led utilisation of pressure support ventilation (PSV), referenced to four reported conventional screening criteria hypothesising that these criteria would have delayed the weaning progress.

Methods: A prospective observational cohort study of adult patients receiving MV in a 30-bed university hospital intensive care unit (ICU). Logistic regression analysis identified factors associated with PSV failure. Outcome is reported according to adherence to the screening criteria.

Results: 209 patients were included (age 62.6 ±15.9 years, male:female 115:94, Acute Physiology and Chronic Health Evaluation (APACHE) II 16.7±6.1). Median (IQR) time to initiate PSV was 11.0 (5.0-22.0) h, and duration of weaning to extubation was 43.0 (13.0-121.5) h. PSV weaning was initiated despite significant hypoxia (partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO₂:FiO₂) 35.8 ±15.9 kPa), moderate positive end-expiratory pressure levels (7.5±2.5 cm H₂O), deep sedation (44% Richmond Agitation and Sedation Scale (RASS) ≤ -3) and cardiovascular instability (48.8%). At PSV initiation, 85% of patients violated at least one screening criterion, yet 74.6% of patients remained stable for 24 h and 25.4% of patients were successfully extubated within 12 h. There was no association between individual screening criteria and PSV failure. Failure to sustain a PSV trial was associated with ventilation >7 days (RR=2.12 (1.33 to 3.38), p=0.002) and ICU mortality (RR=2.94 (1.46 to 5.94), p=0.002)

Conclusions: Physician-led transition to PSV and weaning was often initiated early and successfully before patients fulfilled conventional screening criteria. Failure to sustain a PSV trial could be an early indicator of prolonged MV and ICU mortality and warrants further investigation. These data support the view that current screening criteria may delay initiation of weaning.

KEY MESSAGES

- Recognising the earliest time point when weaning from mechanical ventilation can be attempted has significant potential clinical benefit.
- Conventional screening criteria for determining readiness-to-wean including hypoxia, levels of positive end expiratory pressure, sedation score and cardiovascular stability may delay weaning progress.
- Physician-led weaning to pressure support ventilation is often initiated early and successfully prior to patients meeting conventional screening criteria.

INTRODUCTION

Weaning describes the process of liberation from mechanical ventilatory support.¹ Following adequate treatment of the cause of acute respiratory failure, the clinician must make an assessment of the patient's readiness to wean.¹ Delay in appreciation and assessment of readiness to wean are key factors contributing to prolonged mechanical ventilation (MV) with adverse consequences on the intensive care unit (ICU) length of stay, ICU-related complications and healthcare-associated costs.² Recognising the earliest time point when weaning can be attempted has significant potential clinical benefit, although weaning practices vary significantly internationally.⁸

In patients who cannot undergo immediate ventilator liberation following an initial spontaneous breathing trial (SBT), current evidence suggests that ventilator weaning is best performed either by repeated SBTs or by gradual reduction in pressure support ventilation (PSV).^{4 5} Weaning trials and guidelines commonly apply screening criteria, which must be fulfilled to determine the clinical stability of patients before weaning can be started.^{1 2 4–10} In these trials, weaning occurs in series with resolution of the underlying illness. Typical screening criteria include measurement of partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO₂:FiO₂) >26.3 kPa, positive end-expiratory pressure (PEEP) \leq 5 cm H₂O and no requirement for vasoactive drugs or sedation. However, the clinical utility of these criteria has never been validated. If these criteria are too prescriptive, then close adherence could potentially delay weaning, by excluding patients who may otherwise successfully wean if attempted. This issue is highlighted in the seminal work of Esteban *et al*^{$\check{p}}$ which employed</sup> standard weaning criteria and, in a cohort with modest illness severity, reported that weaning did not start for over 1 week. Furthermore, in the trial of Ely *et al*,² by the time-screening criteria were fulfilled in their cohort, the majority could be immediately extubated, suggesting that a positive SBT could have been achieved at an earlier stage. Indeed, in a broader context, the role of protocols in the weaning process is not clear.^{2 8 11}

The aim of this study was to observe the practice of physician-led weaning using the PSV mode, referenced to four conventional screening criteria for weaning, to assess efficacy, adherence and outcome. We investigated the factors associated with failure to establish PSV and hypothesised that adherence to these conventional screening criteria would have delayed the weaning process.

METHODS

Study design and ethical approval

This was a non-interventional, prospective, observational cohort study of sequential critically ill adult patients (\geq 18 years of age) conducted in two 15-bedded, mixed medical–surgical ICUs of a large university teaching hospital between August 2005 and April 2007. Recruitment was pragmatic, occurring over a predefined time frame, with no a priori sample size determined. The study was approved by the institutional ethics review board of the hospital that waived the requirement for informed consent from patients. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies have been followed in the reporting of this study.¹²

Patients

Patients were eligible for inclusion if they underwent initiation of invasive MV (via an endotracheal tube) in the ICU. Exclusion criteria were in keeping with previous weaning trials and included age <18 years, pregnancy, requirement for high-dose vasoactive drugs (epinephrine or norepinephrine $\geq 0.5 \,\mu\text{g/kg/min}$), patients transferred from another ICU and short-stay patients from the postoperative overnight intensive recovery unit (which includes elective cardiac and other surgical patients requiring elective postoperative ventilation), a 'do not attempt resuscitation' order, patients receiving chronic domiciliary non-invasive ventilation and patients with a primary neurological cause of ventilator dependence (including a Glasgow Coma Scale ≤ 12 with no or minimal sedation and postcardiac arrest with poor neurological prognosis).

Ventilation and sedation practice on the ICUs

Each ICU is staffed by one consultant critical care physician and three junior critical care physicians, with a 1:1 nurse-to-patient ratio. Ventilator management is physician-led and nurse facilitated without formal weaning protocols. Ventilators in use during the study period were the Dräger Evita XL (without use of the SmartCare software; Dräger Medical, Lübeck, Germany) and Viasys Avea (CareFusion Corporation, San Diego, California, USA). PSV was initiated at the discretion of the treating clinician according to clinical judgement. Patients were reviewed on three formal ward rounds daily where weaning plans were instituted, reviewed or modified in accordance with clinical assessment.

The default PSV set-up was as follows: flow triggering with sensitivity 2.0 L/min; automatic tube compensation turned on with information on airway type (endotracheal tube vs tracheostomy) and airway internal diameter provided; ramp time 0.2 s; cycling off at 25% of peak inspiratory flow. Pressure support level was set to maintain a comfortable respiratory pattern for the patient and to achieve appropriate targets for respiratory rate, tidal volume and/or blood gases as prescribed by the medical staff. Extubation was not protocolised but typical practice would be to extubate once the patient was stable on minimal ventilator requirements (typically PSV 5/5 cm H₂O or less) provided the patient was awake and cooperative, with adequate cough and manageable secretions. The standard sedation regime uses propofol and fentanyl, titrated by infusion to a Richmond Agitation and Sedation Scale (RASS)¹³ as prescribed by the medical team. Although there was no explicit sedation protocol in place, clinicians completed a daily checklist which included a prompt to perform a sedation hold unless contraindicated.

Data collection

A prospective dataset was collected by an independent research nurse. This included demographics, indication for MV, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score; sedation dose and assessment (RASS); time from ICU admission to initiate PSV; time from ICU admission to liberation from MV (defined as successful extubation or disconnection from MV via a tracheostomy for >24 h); ventilator settings; arterial blood gas values and haemodynamic variables immediately before, immediately after and 24 h after initiating PSV; rates of adverse events (failure of PSV trial, reintubation, tracheostomy and ICU mortality) and total duration of MV.

Weaning criteria and failure of PSV

The four conventional screening criteria were defined as PaO_2 :FiO₂ ratio >26.3 kPa, PEEP \leq 5 cm H₂O, RASS \geq 3 (more awake than 'moderate sedation') and cardiovascular stability, to be referred to as 'conventional criteria'. Cardiovascular stability was defined as heart rate <120 bpm and mean arterial pressure >65 mm Hg with no requirements for vasoactive drugs by continuous infusion. Respiratory acidosis was defined as pH <7.3 and partial pressure arterial carbon dioxide (PaCO₂) >6 kPa.

Failure of the PSV trial was defined as both a clinical deterioration requiring restart of a mandatory controlled ventilation mode within the first 24 h after initiation of PSV. As this was a non-interventional study of non-protocolised weaning practice, this management was at the discretion of the clinical team, for example, due to hypoventilation, rapid shallow breathing unresponsive to titration of pressure support or deterioration in pulmonary gas exchange.

Statistical analysis

Continuous variables are presented as mean±SD and median (IQR) as appropriate. Categorical variables are presented as n (%). Statistical analysis was performed using STATA (StataCorp 2009. Stata Statistical Software: Release 11. College Station, Texas, USA: StataCorp LP). We performed logistic regression analysis to identify factors independently associated with PSV failure using a stepwise backward approach specifying the likelihood ratio test as a test of term significance. We started from the full model, which includes all the variables (except PaCO₂ and respiratory acidosis, removed to avoid multiple collinearity), setting the retaining criteria as a p value ≤ 0.05 . For variables that did not reach statistical significance in the multivariate analysis, we have reported the p value only.

RESULTS

Cohort demographics

In total, 209 sequential patients were included. Baseline demographic data for the cohort are reported in table 1. There were similar proportions of medical and surgical patients with a high rate of cardiovascular and respiratory comorbidity and moderate sickness severity. Causes of respiratory failure included chronic obstructive pulmonary disease (n=30), pneumonia (n=40), congestive cardiac failure/other cardiac problems (n=15), pulmonary haemorrhage (n=3) and aspiration (n=3). Other causes of admission included sepsis or multiorgan failure, gastro-intestinal bleeding or emergency postoperative care.

Duration of the phases of MV

All 209 patients underwent initiation of weaning in PSV, with time to change from controlled mandatory ventilation to PSV of 11.0 (5.0-22.0) h (table 2). Of the total duration of MV, 80.7% was in PSV mode. Fifty-three patients (25.4%) were extubated within 12 h of

Table 1 Demographic data for study cohort				
Demographic	Sample			
Age (years)	62.6±15.9			
Sex (M:F)	115:94			
APACHE II (ICU admission)	16.7±6.1			
Admission category				
Medical	100 (48)			
Emergency surgical	67 (32)			
Elective surgical	42 (20)			
Comorbidity				
Cardiac disease	74 (35)			
Chronic respiratory disease	58 (28)			
Chronic renal disease	16 (8)			
Immunocompromise	16 (8)			
Chronic liver disease	11 (5)			
Active malignancy	6 (3)			
Data are presented as mean±SD or n (%) where appropriate. n=209.				
APACHE II, Acute Physiology and Chronic Health Evaluation; F, female; ICU, intensive care unit; M, male.				

transition to PSV, and duration of weaning in PSV mode until extubation was 43.0 (13.0–121.5) h. A small proportion of patients required prolonged periods of controlled ventilation and prolonged weaning in PSV.

Following transition to PSV, active weaning began with a median decrease in pressure support of 5.5 (2–10) cm H_2O in the first 24 h. In total, 25.4% of patients fulfilled the criteria for failure of the PSV trial due to clinical deterioration requiring conversion back to controlled ventilation within the first 24 h.

Table 2	Duration of	phases of	MV, ra	ates of	adverse
events ar	nd outcomes	5			

Duration of phases of MV and				
weaning	n			
Intubation to initiation of PSV (h)	11.0 (5.0–22.0)			
Initiation of PSV to extubation (h)*	43.0 (13.0–121.5)			
Total duration of MV (h)	67.0 (25.5–156.5)			
Proportion of all MV time in PSV	80.7%			
mode				
Outcomes				
Reduction in pressure support for	5.5 (2.0–10.0)			
patients who remained in PSV for				
24 h (cm H ₂ O)				
Failure to remain in PSV mode at	53 (25.4)*			
24 h				
Failed extubation	34 (16.3)*			
Failed extubation >1 occasion	6 (2.9)*			
Tracheostomy	32 (15.3)*			
ICU LOS (days)	6.0 (3.0–12.0)			
ICU mortality	26 (12.4)*			
Data are presented as median (IQR), n (%)* or per cent as				
appropriate. n=209.				
*n=188, as 21 patients died prior to extubation.				

ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilation; PSV, pressure support ventilation.

Physiological parameters and organ support at initiation of PSV

The RASS, doses of sedation, PaO_2 :FiO₂, PEEP, arterial blood gas values, cardiovascular parameters and Sequential Organ Failure Assessment (SOFA) scores at initiation of PSV are shown in table 3. PSV weaning was initiated despite significant hypoxia (PaO₂:FiO₂ 35.8 ±15.9 kPa), moderate PEEP levels (7.5±2.5 cm H₂O), deep sedation (44% RASS \leq 3) and cardiovascular instability requiring vasopressors (48.8%).

Fifty-six per cent of patients utilised bilevel positive airway pressure prior to PSV initiation, and 44% utilised synchronised intermittent mandatory ventilation (usually pressure regulated volume control). The pH and PaCO₂ were 7.35 \pm 0.07 and 5.7 \pm 1.3 kPa, respectively. Forty-two per cent of the patients were receiving infusions of vasoactive drugs. There was only a weak association between baseline APACHE II score and time to initiate PSV (r=0.22; p=0.002).

Rates of adherence to conventional criteria

At the time of PSV initiation, 85% of patients violated at least one screening criterion, yet 74.6% remained stable

Table 3 Physiological parameters and organ support at initiation of PSV					
Neurological					
RASS	−2 (−2 to −3)				
RASS –5	2 (1)				
RASS –4	18 (9)				
RASS –3	70 (34)				
Sedation in 24 h prior to PSV					
Propofol (mg)	730 (240–1690)				
Fentanyl (µg)	400 (0–1175)				
Respiratory					
PaO ₂ :FiO ₂ (kPa)	35.8±15.9				
PEEP (cm H ₂ O)	7.5±2.5				
рН	7.35±0.07				
PaCO ₂ (kPa)	5.7±1.3				
Cardiovascular					
HR (bpm)	88±17				
MAP (mm Hg)	77±11				
Requiring vasoactive drugs	88 (42)				
SOFA*					
SOFA (total)	6 (4–8)				
Respiratory	1 (1–3)				
Cardiovascular	1 (1–3)				
Renal	0 (0–2)				
Hepatic	1 (0–1)				
Haematological	0 (0–2)				
GCS†	0 (0–0)				

Data are presented as mean \pm SD or median (IQR). n=209. *n=199.

†Assumed GCS not accounting for sedation.

FiO₂, fraction of inspired oxygen; GCS, Glasgow Coma Scale; HR, heart rate; MAP, mean arterial pressure; PaCO₂, partial pressure arterial carbon dioxide; PaO₂, partial pressure arterial oxygen; PEEP, positive end-expiratory pressure; PSV, pressure support ventilation; RASS, Richmond Agitation and Sedation Scale; SOFA, sequential organ failure assessment. for 24 h (table 2). Adherence rates to the conventional criteria are shown in table 4. Nearly two-thirds of patients did not meet the PEEP criterion, and almost half would have failed the neurological and cardiovascular screening.

Clinical parameters associated with PSV failure

Multivariate logistic regression analysis demonstrated that of the factors analysed, only preweaning arterial pH (RR 0.996 (0.993 to 0.998), p=0.002) was associated with PSV failure (table 5). Failure to adhere to the conventional criteria (PaO₂:FiO₂ <26 kPa, PEEP >5 cm H₂O, RASS \leq 3, cardiovascular instability) was not associated with PSV failure. Furthermore, PSV failure was not associated with age, APACHE II, presence of chronic respiratory and cardiovascular disease or time to initiate PSV. For completeness, additional analysis was performed correcting for missing values using the hotdeckvar algorithm, implemented in STATA, but this did not change the overall results.

Relationship between failure of PSV trial and clinical outcome

Failure to sustain PSV for 24 h was associated with prolonged duration of MV >7 days (RR=2.12 (1.33 to 3.38), p=0.002) and ICU mortality (RR=2.94 (1.46 to 5.94), p=0.002).

DISCUSSION

Data from this prospective observational cohort study demonstrated that in a cohort of mixed medical and surgical ICU patients managed without a weaning protocol, PSV initiated early in the course of MV, prior to fulfilment of conventional screening criteria for weaning, was well tolerated in the majority of patients. The four individual and specific criteria, similar to those commonly applied in weaning trials and guidelines, were not associated with PSV failure. Acidosis at the time of initiation of PSV was the only factor independently associated with PSV failure. Failure to maintain PSV for 24 h was

 Table 4
 Rates of adherence to conventional criteria for initiation of weaning at time of pressure support ventilation initiation

Conventional criterion	Conventional level for initiating weaning	Study patients not meeting criterion
PaO ₂ :FiO ₂ (kPa)	>26	62 (30)
PEEP (cm H ₂ O)	≤5	127 (61)
RASS	≥3	90 (43)
Cardiovascular stability	Stable	102 (49)

n=209. Data are presented as n (%).

PaO₂,partial pressure arterial oxygen; PEEP, positive

end-expiratory pressure; RASS, Richmond Agitation and Sedation Scale.

Table 5	Logistic red	gression a	nalysis of	independent	t risk factors	s for PSV failure

	Univariate analysis		Multivariate analysis		
Parameter	OR (95% CI)	p Value	OR (95% CI)	p Value	
Age (years)	1.002 (0.983 to 1.022)	0.83		0.77	
APACHE II	1.035 (0.984 to 1.089)	0.18		0.61	
Chronic respiratory disease	1.037 (0.519 to 2.075)	0.92		0.76	
Chronic cardiovascular disease	0.731 (0.374 to 1.428)	0.36		0.8	
Time to initiation of PSV (h)	0.996 (0.982 to 1.011)	0.63		0.57	
RASS ≤3	1.533 (0.819 to 2.868)	0.18		0.54	
PEEP >5 cm H_2O	1.513 (0.783 to 2.923)	0.22		0.52	
PaO ₂ :FiO ₂ ≤26 kPa	1.841 (0.955 to 3.546)	0.07		0.1	
рН	0.996 (0.993 to 0.998)	0.002	0.996 (0.993 to 0.998)	0.002	
PCO ₂ (kPa)	1.146 (0.911 to 1.441)	0.24			
Respiratory acidosis	2.060 (0.835 to 5.083)	0.12			
Cardiovascular instability	1.829 (0.969 to 3.451)	0.06		0.06	

n=196. Missing data point for one of the predicting variables n=13.

APACHE II, Acute Physiology and Chronic Health Evaluation; FiO₂, fraction of inspired oxygen; PaCO₂, partial pressure arterial carbon dioxide; PaO₂, partial pressure arterial oxygen; PEEP, positive end-expiratory pressure; PSV, pressure support ventilation; RASS, Richmond Agitation and Sedation Scale.

associated with prolonged MV and increased ICU mortality and thus has the potential to be used as an important screening tool to identify high-risk patients.

These data add to the current literature on PSV as a ventilatory support mode as well as a weaning mode. Previous studies of PSV as a support mode have been relatively small and have commonly examined physiological rather than clinical endpoints.^{14–17} Although use of PSV may represent common practice, it has not been systematically reported. Indeed, a large prospective cohort study found less than 20% of patients in PSV mode up to 28 days after the onset of MV.¹⁸

Critique of the method

Despite screening all admissions into the ICU over a 20-month period, the sample size is limited by strict exclusion criteria. While this defines the cohort clearly, it may limit the generalisability of this single-centre study. In particular, caution should be applied in extrapolating these results to patients with severe cardio-vascular instability and those with a primary neurological cause of ventilator dependence. Nevertheless, the impact of sickness severity on weaning initiation and PSV tolerance was modest, and overall the exclusion criteria and the sickness severity in our cohort were similar to other weaning studies.^{4 5}

This study may be criticised for equating PSV initiation with the start of weaning. It is recognised that disagreement may exist over the definition or practice of weaning.¹⁹ It was not our practice to systematically apply an SBT to assess for ability to achieve immediate ventilator separation and we cannot exclude that had we done so, some patients could have been extubated immediately at the time of transition to PSV. Had this been the case, it would further reinforce the view that these criteria should not preclude assessment for ventilator separation. In addition, our selection of criteria to determine readiness to wean was based on those previously reported in the literature, and which were objective and easily quantifiable for the research setting. It is possible that the use of alternative, broader criteria may have resulted in different findings, although some criteria such as adequate cough, minimal secretions or absence of sepsis are more subjective in nature with the potential to introduce bias in the data acquisition process.

The results of this study may be confounded by factors not analysed; for example, physiological (eg, high-grade fever), diagnostic (eg, delirium or ventilator-associated pneumonia) or logistic variables (eg, transfer to imaging department), which could have led to the primary outcome (clinical deterioration requiring the restart of mandatory ventilation) but which were not directly related to weaning failure per se. Additionally, we cannot be certain that PSV was applied optimally for all patients, in terms of, for example, minimising asynchrony.^{20 21} Furthermore, it is possible that clinicians' practice may have been influenced by knowledge of an observational weaning study within the ICU, but we sought to reduce this by collecting data remotely using a clinical information system. Finally, as this was an observational study, associations identified do not necessarily imply causality and these data can only be hypothesis generating to inform prospective studies. Further studies of alternative modes of ventilation that allow for patient contribution may also be beneficial.

Early initiation of PSV and adherence to conventional criteria

In this study, the time to initiate PSV was short and was only minimally influenced by sickness severity on admission. PSV initiation and weaning occurred despite deep levels of sedation, significant hypoxia, moderate PEEP levels and cardiovascular instability, and indeed only a small proportion of the patients fulfilled all four of the conventional screening criteria. Despite this, PSV was well tolerated in the majority with three quarters remaining in PSV, with clinically significant reductions in the level of pressure support in the first 24 h and with a low overall mortality of 12.4%. These findings highlight the potentially restrictive nature of predefined screening criteria if they are rigorously applied, irrespective of clinical judgement. Early initiation of spontaneous breathing may be associated with benefits including a reduction in sedation requirements, limiting ventilator-induced diaphragmatic dysfunction, improved regional ventilation of dorsal lung units and improved cardiovascular status.^{22–24}

Clinical parameters associated with PSV failure

Violation of any individual conventional criteria was not associated with PSV failure. The only factor significantly associated with PSV failure was arterial pH level, and as there was no association with PaCO₂ or respiratory acidosis, this suggests that metabolic acidosis was the key factor, a clinically plausible suggestion due to the respiratory load associated with compensation. It is notable that even patients who were assessed as moderately to deeply sedated tolerated PSV, because it is intuitive that respiratory drive is linked to sedation score. However, our data are consistent with the Awakening and Breathing Controlled trial²⁵ which found no difference in tolerance to an SBT in patients who were awake or not. In our study, the doses of sedation were relatively low and the use of short-acting drugs by infusion may have allowed rapid sedation adjustment titrated against respiratory drive. It is unclear whether similar results would be obtained if sedation was administered with longer acting sedation regimes.

Clinical predictive value of PSV trial

Approximately one-quarter of patients failed to sustain PSV for 24 h and this was associated with a subsequent prolonged duration of MV and increased ICU mortality. Future investigation could determine the predictive characteristics of such findings, that is, sensitivity and specificity, which may further validate the clinical significance of a failed PSV trial. These data are consistent with those previously reported demonstrating an increased duration of ventilation in patients with acute lung injury who failed a PSV trial.²⁶ An early trial of PSV could risk stratify patients, specifically identifying those who are at risk of being in a 'prolonged weaning' category¹ which correlates with mortality.²⁷ This could alert clinicians to consider early interventions which attempt to moderate the adverse effects of prolonged ventilation including early targeted physical rehabilitation²⁸ and/or tracheostomy to facilitate earlier ventilator separation.^{29 30} Nevertheless, PSV failure alone is of insufficient predictive value to determine which patients will require prolonged ventilation and other factors should also be considered.^{30 31} It has been suggested that spontaneous breathing may be harmful in some patients, for example, with acute respiratory distress syndrome (ARDS)³² ³³ and whether failure of a PSV trial contributes to adverse outcome or rather that the PSV trial is acting as a physiological stress test cannot be confirmed from this study. This should be an area of further study.

CONCLUSION

In this observational cohort study of physician-led weaning practice in a large university ICU, PSV was initiated early in the course of MV, even in patients with high levels of sickness severity and with the majority not meeting conventional criteria for weaning. Despite this, PSV was well tolerated in a large proportion of the cohort with active weaning of pressure support and a significant rate of early extubation achieved. Furthermore, the conventional screening criteria (as interpreted and applied in this study) did not predict PSV failure. Acidaemia is associated with failure to sustain PSV and this should be heeded by clinicians before weaning from the ventilator and may be considered in future weaning trials and guidelines. Failure to sustain a PSV trial for 24 h may be considered as a clinical indicator of patients who are at increased risk of prolonged MV and mortality, and the predictive test characteristics of this as a clinical tool would be important to determine. Early transition to PSV appears safe and effective in the majority of patients. Rigorous application of strict screening criteria, often reported in the literature, may delay initiation of weaning in a cohort of patients, with clinical and healthcare utilisation implications.

Contributors GG was responsible for study inception and design, data analysis and interpretation, manuscript preparation and editing as well as intellectual oversight. BC undertook manuscript preparation, editing and submission. SDG and MT completed statistical analyses. LA performed data acquisition. RB contributed to study design and intellectual oversight. NH contributed to study design, data interpretation and manuscript editing.

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REFERENCES

- 1. Boles JM, Bion J, Connors A, *et al.* Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033–56.
- Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335:1864–9.

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- Burns K, Raptis S, Bakshi J, et al. Practice variation in weaning critically ill adults from invasive mechanical ventilation: preliminary results of an international survey. Am J Respir Crit Care Med 2011;183:A6247.
- Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am. J Respir Crit Care Med 1994;150:896–903.
- Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. N Engl J Med 1995;332:345–50.
- Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Am J Respir Crit Care Med 1997;156:459–65.
- Kollef MH, Shapiro SD, Silver PM, *et al.* A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. *Crit Care Med* 1997;25:567–74.
- Krishnan JA, Moore D, Robeson C, *et al.* A prospective, controlled trial of a protocol-based strategy to discontinue mechanical ventilation. *Am J Respir Crit Care Med* 2004;169:673–8.
- Lellouche F, Mancebo J, Jolliet P, et al. A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. Am J Respir Crit Care Med 2006;174:894–900.
- Rose L, Presneill J, Johnston L, *et al.* A randomised, controlled trial of conventional versus automated weaning from mechanical ventilation using SmartCare[™]/PS. *Intensive Care Med* 2008;34:1788–95.
- Blackwood B, Alderdice F, Burns K, *et al.* Use of weaning protocols for reducing duration of mechanical ventilation in critically ill adult patients: Cochrane systematic review and meta-analysis. *BMJ* 2011;342:c7237.
- 12. von Elm E, Altman D, Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61:344–9.
- 13. Sessler CN, Gosnell MS, Grap MJ, *et al.* The Richmond Agitation– Sedation Scale. *Am J Respir Crit Care Med* 2002;166:1338–44.
- 14. Aliverti A, Carlesso E, Dellaca R, *et al.* Chest wall mechanics during pressure support ventilation. *Crit Care* 2006;10:R54.
- Ferrer M, Iglesia R, Roca J, *et al.* Pulmonary gas exchange response to weaning with pressure-support ventilation in exacerbated chronic obstructive pulmonary disease patients. *Intensive Care Med* 2002;28:1595–9.
- Patroniti N, Foti G, Cortinovis B, et al. Sigh improves gas exchange and lung volume in patients with acute respiratory distress syndrome undergoing pressure support ventilation. *Anesthesiology* 2002;96:788–94.
- Zeravik J, Borg U, Pfeiffer UJ. Efficacy of pressure support ventilation dependent on extravascular lung water. *Chest* 1990;97:1412–19.

- Esteban A, Anzueto A, Frutos F, *et al.* Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002;287:345–55.
- 19. Hess DR, MacIntyre NR. Ventilator discontinuation: why are we still weaning? Am J Respir Crit Care Med 2011;184:392–4.
- Chiumello D, Pelosi P, Taccone P, *et al.* Effect of different inspiratory rise time and cycling off criteria during pressure support ventilation in patients recovering from acute lung injury. *Crit Care Med* 2003;31:2604–10.
- Thille A, Cabello B, Galia F, *et al.* Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation. *Intensive Care Med* 2008;34:1477–86.
- Gayan-Ramirez G, Testelmans D, Maes K, *et al.* Intermittent spontaneous breathing protects the rat diaphragm from mechanical ventilation effects *. *Crit Care Med* 2005;33:2804–9.
- 23. Jaber S, Petrof BJ, Jung B, *et al.* Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. *Am J Respir Crit Care Med* 2011;183:364–71.
- 24. Putensen C, Muders T, Varelmann D, *et al.* The impact of spontaneous breathing during mechanical ventilation. *Curr Opin Crit Care* 2006;12:13–18.
- Girard TD, Kress JP, Fuchs BD, *et al.* Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet* 2008;371:126–34.
- Cereda M, Foti G, Marcora B, et al. Pressure support ventilation in patients with acute lung injury. Crit Care Med 2000;28:1269–75.
- Peñuelas O, Frutos-Vivar F, Fernández C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med 2011;184:430–7.
- Burtin C, Clerckx B, Robbeets C, *et al.* Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 2009;37:2499–505.
- Terragni P, Antonelli M, Fumagalli R, et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: a randomized controlled trial. JAMA 2010;303:1483–9.
- Young D, Harrison D, Cuthbertson B, *et al.* Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: the TracMan randomized trial. *JAMA* 2013;309:2121–9.
- Estenssoro E, González F, Laffaire E, *et al.* Shock on admission day is the best predictor of prolonged mechanical ventilation in the ICU. *Chest* 2005;127:598–603.
- Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010;363:1107–16.
- Schmidt U, Hess D. Does spontaneous breathing produce harm in patients with the acute respiratory distress syndrome? *Respir Care* 2010;55:784–6.